

REMARKS

Request for Extension of Time

Applicants, through their undersigned attorney, respectfully request a one-month extension of time for responding to the Communication mailed 7 August 2006, in the above-identified patent application. The time for response is thus extended up to and including 7 December 2006.

The amendments set out above and the following remarks are believed responsive to the points raised by the Examiner in the Office Action dated 9 August 2006. Entry of the above is respectfully requested. Any changes made to the specification or claims by entry of this amendment are shown in the attached sheet, in accordance with 37 C.F.R. 1.121.

Following the entry of this amendment claims 37-40 and 50-54 are pending. In view of the amendments set out above and the following remarks, reconsideration is respectfully requested.

The following comments address the points raised by the Examiner in the order they are presented in the Official Action.

Priority

To address the issues raised in the office action, please find attached an ADS appropriate for this application, as required by 37 C.F.R. 1.78(a).

Concerning the 35 U.S.C. 112, Second Paragraph rejection of Claims 38-40

Claims 38-40 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim 38 has been amended to delete "heterologous," therefore providing antecedent basis for "a bacteriocin."

Regarding Claim 40, Applicants respectfully request reconsideration for using the phrase "an operable mutein thereof." Applicants submit that the phrase is not indefinite to one skilled in the art, and furthermore, is easily discernible using the teachings in the

specification.

First, mutein is defined at page 14, line 25+ as a "conservative variation" and provides as an example a difference of "1-4 amino acid residues." Most importantly, the muteins "must exhibit bacteriocinogenic activity (page 15, line 1), regardless of the number of differences between the mutein and the native divergicin A processing peptide. We suggest one skilled in the art would readily recognize this teaching in the specification as including variations that result in an expression vector that produces a bacteriocin that kills target bacteria.

Secondly, the invention is described in the specification, in part, as an expression system for expressing a bacteriocin in a lactic acid bacterium host. See for example, page 3, lines 25+, and page 4, lines 3-9. As noted at page 19, lines 5-7, a major consequence of the discoveries that underpin the invention is the ability to express a gram negative bacteriocin (e.g., colicin V) in a gram positive host (e.g., lactic acid bacteria). Applicants therefore suggest that an operable mutein is any sequence that functions in the gram positive host to produce a gram negative bacteriocin. As the examples show, creating and determining that a particular mutein of divergicin A is routine and simple. Merely insert it in the expression system, and the bacteriocin is expressed or it is not. If not, then it can not be an "operable mutein thereof" as required by claim 38.

Thus, in light of the foregoing remarks, Applicants submit that the rejection has been overcome so as to point out and distinctly claim the subject matter that Applicants regard as their invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 112, second paragraph rejection of claims 38-40.

Concerning the 35 U.S.C. 112, First Paragraph rejection of Claims 38-40

Claims 38-40 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Claims 38-40 have been rejected for their inclusion of "an operable mutein thereof" in claim 38. Reconsideration is respectfully requested.

Applicants respectfully request reconsideration because 1) Applicant can

demonstrate why the written description is adequate to support the claims; and 2) the failure to follow the Patent Office's own Guidelines in supporting the rejection.

Applicants respectfully submit that one skilled in the art would readily recognize what is meant by "an operable mutein thereof." This area of recombinant DNA processing is a mature field, and in expression vectors, whether a vector works or does not is easily verified. It either expresses the bacteriocin, or it does not. If a bacteriocin is expressed, it is either functional, or it is not.

Applicants have supplied the sequence of the divergicin A processing peptide. If one skilled in the art uses a mutant divergicin A processing peptide, it can be easily compared to the sequence provided by applicants, and whether it is expressed is easily determined, well within the capability of one of even average skill in the art, and is taught throughout the specification (see for example the top of page 61, which teaches a bacteriocin activity assay). If the mutein is either not expressed or is not functional, this assay easily indicates that the mutein is not operable.

We therefore suggest that one skilled in the art, having the sequence of divergicin A peptide and the test for determining expression and activity (all supplied by the specification), must conclude that applicants were in possession of invention. The sequence plus the defined activity shows that applicant was in possession of the necessary common attributes possessed by members of the genus called for in applicants claim.

Further, under the Guidelines for the Examination of Patent Applications Under 35 U.S.C. 112, Paragraph 1 Written Description Requirement, "the examiner has the initial burden ... of presenting evidence or reasons why a person skilled in the art would not recognize that the written description provides support for the claims" (66 Fed. Reg. 1099). The absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. 112, para. 1, for lack of adequate written description. Also, the reasoning "should be supported by a reference, rather than by taking "notice," because the interpretation is the principle evidence supporting the rejection. See MPEP 2144.03 (For further views on official notice, see *In re Ahlert*, 424 F.2d 1088, 1091 165 USPQ 418, 420 - 421 (CCPA 1970) ("[A]ssertions of technical

facts in areas of esoteric technology must always be supported by citation of some reference work" and "allegations concerning specific 'knowledge' of the prior art, which might be peculiar to a particular art should also be supported." Furthermore the applicant must be given the opportunity to challenge the correctness of such assertions and allegations. "The facts so noticed serve to 'fill the gaps' which might exist in the evidentiary showing" and should not comprise the principle evidence upon which a rejection is based.); see also, *In re Barr*, 444 F.2d 588, 170 USPQ 330 (CCPA 1971) (scientific journal references were not used as a basis for taking judicial notice that controverted phrases were art – recognized because the court was not sure that the meaning of the term at issue was indisputable among reasonable men); *In re Eynde*, 480 F.2d 470, 178 USPQ 46, 470,474 (CCPA 1973) ("The facts constituting the state of the art are normally subject to the possibility of rational disagreement among reasonable men and are not amenable to the taking of [judicial] notice.").)

Applicants respectfully submit that the Examiner was required to provide evidence to support the reasoning, particularly in light of the prior art submitted by Applicant and used by the Examiner in the office action, by the extensive description in the specification of the expression and activity of the bacteriocins, and by the operative examples providing a species that is representative of the genus.

Reconsideration is respectfully requested.

Concerning the 35 U.S.C. 102(a) rejection of Claims 37-39

Claims 37-39 have been rejected under 35 U.S.C. 102(a) as being anticipated by McCormick et al.

Reconsideration is respectfully requested. This reference was published in Nov. 1996, and applicants' claim of priority extends back to the original provisional application that was filed on 5 September 1996. Applicants therefore respectfully suggest that this reference is not available as a reference against the claims.

Concerning the 35 U.S.C. 102(a) rejection of Claims 37-39

Claims 37-39 have been rejected under 35 U.S.C. 102(a) as anticipated by

Worobo, et al. Reconsideration is respectfully requested.

In contrast to the characterization in the office action of what Worobo teaches, Worobo does not actually teach ALL of the claim elements in a single construct. Worobo teaches a first construct, pRW5.6 (page 3145 last paragraph), that contains the p59 promoter (from pGKV259) and the structural gene for divergicin A (the 514-bp EcoRV-AccI fragment, in the first ORF of pCD3.4). This construct does NOT include a "second polynucleotide encoding a bacteriocin processing peptide."

The second construct taught in Worobo teaches a bacteriocin processing peptide, but it does NOT teach this processing peptide in the expression of a bacteriocin (the construct on page 3146 under the heading "Alkaline phosphatase fusion" expresses alkaline phosphatase, which is not a bacteriocin).

Because claim 37 calls for a bacteriocin polynucleotide and a processing polynucleotide in the same construct, it is respectfully submitted that the reference fails to teach the claimed invention.

35 U.S.C. 103(a) rejection over either McCormick or Worobo

The Official Action rejected claim 40 under 35 U.S.C. §103(a) as unpatentable over either McCormick or Worobo. The rejection is respectfully traversed.

Applicants respectfully assert that the Office Action has failed to establish a *prima facie* case of obviousness. The references were not combined in the office action, but were applied separately. First, McCormick is not available as a reference for the reasons noted above. Secondly, Worobo does not teach the expression of a single bacteriocin under the control of a bacteriocin processing peptide, for the reasons noted above. It therefore cannot teach a "plurality of different bacteriocins" as called for in claim 40. Reconsideration is respectfully requested.

Double patenting rejection

Claims 37-40 have been rejected for not being patentably distinct from claims 1-3 of USP 6,403,082. Reconsideration is respectfully requested.

Applicants strongly urge that the claims in the present application are much

broader than claims 103 in Applicants' issued patent. Issued claim 1 calls for "a plurality of different bacteriocins" but claim 37 calls for "a bacteriocin." Issued claims 2 and 3 call for the bacteriocin brochocin C, but none of the claims in applicants' pending application is limited to a particular bacteriocin. Therefore the scope of the pending claims compared to the issued claims is much broader, and therefore clearly patentably distinct.

New claims

New claims 50-54 have been added. No new matter has been included. Basis for claim 50 can be found at page 4, line 5; page 19, line 6; and throughout the specification. Basis for claim 51 can be found at page 11, line 20; the examples; and throughout the specification. Basis for claim 52 can be found at page 10, lines 3+, and throughout the specification. Basis for claim 53 can be found at page 28, line 27, and inherently throughout the specification. Basis for claim 54 can be found in original claim 37; at page 19, lines 4-11; and throughout the specification.

Applicants respectfully suggest that these new claims are patentable for the same reasons noted above for claims 37-40.

Accordingly, in view of the above amendments and remarks, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at 301-203-6300 (a local call).

With the arguments and amendments noted above, it is believed that the previously examined claims are in condition for allowance, and therefore the new claims are also in condition for allowance. Early allowance of the claims is respectfully solicited.

The Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment to Deposit Account No. 02-4650. A duplicate copy of this form is enclosed.

Respectfully submitted,

December 7, 2006

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